


Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/196,154
Filed : November 16, 1995
Page 2

oligosaccharide part and an altered ceramide portion comprising an altered sphingosine base and (ii) Keyhole Limpet Hemocyanin;

b) a saponin derivable from the bark of a Quillaja saponaria Molina tree; and

c) a pharmaceutically acceptable carrier;

the relative amounts of such conjugate and such saponin being effective to stimulate or enhance production in a subject of an antibody to GM2,

 wherein in the conjugate the ganglioside derivative is covalently bound to the Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base of the altered ceramide portion of the ganglioside derivative and the nitrogen of an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin.--

--120. (New) The composition of claim 119, wherein the saponin is QS-21.--

--121. (New) The composition of claim 119, wherein the amount of the conjugate is an amount between about 1 μ g and about 200 μ g.--

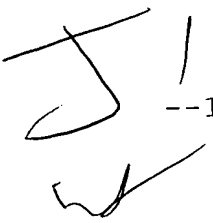
--122. (New) The composition of claim 121, wherein the amount of the conjugate is an amount between 10 μ g and 90 μ g.--

Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/196,154
Filed : November 16, 1995
Page 3

--123. (New) The composition of claim 121, wherein the amount of the conjugate is an amount of between 10 µg and 70 µg.--

--124. (New) The composition of claim 121, wherein the amount of the conjugate is an amount of between 10 µg and 50 µg.--

--125. (New) The composition of claim 119, wherein the amount of the saponin is an amount between about 10 µg and about 200 µg.--

--126. (New) The composition of claim 125, wherein the amount of the saponin is about 100 µg.--

--127. (New) The composition of claim 125, wherein the amount of the saponin is about 200 µg.--

--128. (New) The composition of claim 119, wherein the GM2:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1.--

--129. (New) A composition which comprises:

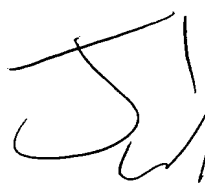
- a) a conjugate comprising (i) a GM2 ganglioside derivative which comprises an unaltered oligosaccharide part and an altered ceramide portion comprising an altered sphingosine base and (ii) Keyhole Limpet Hemocyanin;

Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/196,154
Filed : November 16, 1995
Page 4

b) a saponin derivable from the bark of a Quillaja saponaria Molina tree, wherein the saponin is QS-21; and

c) a pharmaceutically acceptable carrier;

wherein the conjugate is present in an amount between about 10 µg and about 50 µg, the amount of the saponin is about 100 µg, and the GM2:Keyhole Limpet Hemocyanin molar ratio is from 200:1 to 1400:1, where the amount of such conjugate and such saponin is effective to stimulate or enhance production in a subject of an antibody to GM2;

 and wherein in the conjugate the ganglioside derivative is covalently bound to the Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base of the altered ceramide portion of the ganglioside derivative and the nitrogen of an ε-aminolysyl group of Keyhole Limpet Hemocyanin.--


--130. (New) A method of treating a subject afflicted with melanoma which comprises administering to said subject an amount of the composition of claim 129 effective to stimulate or enhance production in a subject of an antibody to GM2 and to thereby treat said melanoma in said subject.--

--131. (New) A method of stimulating or enhancing production of an antibody directed to GM2 in a subject which

Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/196,154
Filed : November 16, 1995
Page 5

comprises administering to the subject an effective amount of a composition which comprises:

- a) a conjugate comprising (i) a GM2 ganglioside derivative which comprises an unaltered oligosaccharide part and an altered ceramide portion comprising an altered sphingosine base and (ii) Keyhole Limpet Hemocyanin;
- b) a saponin derivable from the bark of a Quillaja saponaria Molina tree; and
- c) a pharmaceutically acceptable carrier;

 the relative amounts of such conjugate and such saponin being effective to stimulate or enhance production in a subject of an antibody directed to GM2,

wherein in the conjugate the ganglioside derivative is covalently bound to the Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base of the altered ceramide portion of the ganglioside derivative and the nitrogen of an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin so as to thereby stimulate or enhance production in said subject of the antibody directed to GM2.--

--132. (New) A method of treating a cancer in a subject which comprises administering to the subject an effective cancer treating amount of a composition which comprises:

Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/196,154
Filed : November 16, 1995
Page 6

a) a conjugate comprising (i) a GM2 ganglioside derivative which comprises an unaltered oligosaccharide part and an altered ceramide portion comprising an altered sphingosine base and (ii) Keyhole Limpet Hemocyanin;

b) a saponin derivable from the bark of a Quillaja saponaria Molina tree; and

c) a pharmaceutically acceptable carrier;

the relative amounts of such conjugate and such saponin being effective to stimulate or enhance production in a subject of an antibody to GM2;

51
wherein in the conjugate the ganglioside derivative is covalently bound to Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base of the altered ceramide portion of the ganglioside derivative and the nitrogen of an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin so as to stimulate or enhance production in the subject of the antibody to GM2 and thereby treat the cancer in the subject.--

--133. (New) The method of claim 132, wherein the cancer is of epithelial origin.--

--134. (New) The method of claim 132, wherein the cancer is of neuroectodermal origin.--

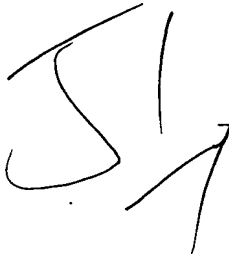
Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/196,154
Filed : November 16, 1995
Page 7

--135. (New) The method of claim 134, wherein the cancer of neuroectodermal origin is a melanoma.--

--136. (New) The method of claim 131 or 132, wherein the administering is effected at two or more sites.--

--137. (New) The method of claim 136, wherein the administering is effected at three sites.--

--138. (New) The method of claim 131 or 132, wherein the composition is administered subcutaneously to said subject.--

--139. (New) The method of claim 138, wherein the composition is administered to said subject at two-week intervals.--

--140. (New) The method of claim 138, wherein the composition is initially administered to said subject at weekly intervals.--

--141. (New) The method of claim 131 or 132, wherein the composition to be administered is prepared prior to administration to the subject by mixing the conjugate and the saponin.--

--142. (New) The method of claim 141, wherein the conjugate and the saponin are mixed on the day of administration to the subject.--

Applicants: Philip O. Livingston and Friedhelm Helling
Serial No.: 08/196,154
Filed : November 16, 1995
Page 8

--143. (New) A method of delaying recurrence of melanoma in subjects at risk of relapse of melanoma which comprises administering to the subject an effective melanoma treating amount of a composition which comprises:

a) a conjugate comprising (i) a GM2 ganglioside derivative which comprises an unaltered oligosaccharide part and an altered ceramide portion comprising an altered sphingosine base and (ii) Keyhole Limpet Hemocyanin;

b) a saponin derivable from the bark of a Quillaja saponaria Molina tree; and

c) a pharmaceutically acceptable carrier;

the relative amounts of such conjugate and such saponin being effective to stimulate or enhance production in a subject of an antibody to GM2,

wherein in the conjugate the ganglioside derivative is covalently bound to Keyhole Limpet Hemocyanin by a stable amine bond between the C-4 carbon of the altered sphingosine base of the altered ceramide portion of the ganglioside derivative and the nitrogen of an ϵ -aminolysyl group of Keyhole Limpet Hemocyanin so as to stimulate or enhance production of an antibody in said subject to GM2 and thereby delay recurrence of melanoma in said subject at risk of relapse of said melanoma.--
